

The Pharmaceutical Industry in Developing Countries

Margriet den Boer and Rafia Morgan

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Abstract / Resumen / Résumé

About a third of the world's population does not have regular access to essential medicines today. This is partly caused by Big Pharma's policies to maintain high drug prices and hold on to exclusive rights for their production, causing them to be completely out of reach for developing countries. But apart from this, there are other ways in which multinational pharmaceutical companies have taken advantage of the situation in poor countries. Clinical trials are conducted according to less strict ethical guidelines than in the West, and old drugs that are potentially dangerous and harmful are actively marketed in the developing world. Much-needed research efforts into tropical diseases are negligible. Activist voices have been stronger than ever before-but do they have enough effect? Can this multi-billion industry be incentivized to spearhead equity and human rights instead of being singularly focused on profit?

En la actualidad, alrededor de un tercio de la población no tiene acceso a los medicamentos esenciales. Esto se debe en parte a las políticas de las grandes farmacéuticas consistentes en mantener unos precios altos y unos derechos de exclusividad de su producción, lo que provoca que ésta quede completamente fuera del alcance de los países en vías de desarrollo. Además, las multinacionales farmacéuticas se han aprovechado de los problemas de los países pobres de manera que se llevan a cabo pruebas clínicas con menos controles éticos que en Occidente y se comercializan medicamentos antiguos potencialmente peligrosos y perjudiciales. Por otra parte, no se acomete la necesidad de investigar en enfermedades tropicales. Pese a que la voz de los activistas es cada vez más poderosa, ¿ha causado algún efecto? ¿Se puede incentivar de algún modo a esta industria que mueve miles de millones para que se ponga al frente de la igualdad y los derechos humanos en lugar de orientarse exclusivamente a la generación de beneficios económicos?

Aujourd'hui, environ un tiers de la population mondiale n'a pas d'accès aux médicaments essentiels. Ceci est dû, en partie, aux politiques suivies par les grandes sociétés pharmaceutiques pour maintenir les prix élevés des médicaments et détenir les droits exclusifs de production, ce qui les rend tout à fait hors de portée pour les pays en voie de déve-

loppement. De plus, les multinationales pharmaceutiques ont utilisé la situation des pays pauvres pour en tirer profit. Ainsi, elles mènent des essais cliniques selon des directives éthiques moins strictes que celles exigées en Occident ; puis elles commercialisent des médicaments potentiellement dangereux et nocifs. En plus, les recherches indispensables sur les maladies tropicales sont négligeables. Les voix des activistes ont été plus fortes que jamais, mais ont-elles assez d'effet ? Serait-il possible d'inciter cette industrie de plusieurs milliards à mener des actions en faveur de l'équité et des droits de l'homme, au lieu d'être singulièrement portée sur les bénéfices ?

Key Words / Palabras clave / Mots-clé

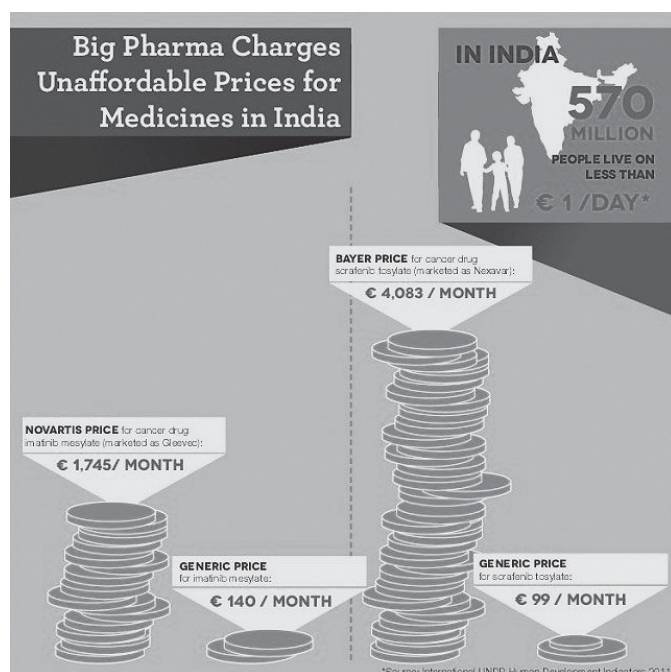
Big Pharma Policies, Developing Countries, Human Rights.

Políticas de las grandes farmacéuticas, países en desarrollo, derechos humanos.

Politiques des grandes pharmaceutiques, pays en développement, Droits de l'Homme.

22 January, 2014: Marijn Dekkers, Dutchman and CEO of Bayer ('Science for a Better Life'), made a statement in a public forum that went viral over the internet and caused outrage among activists. Bayer marketed a new cancer drug called Nexavar in India for over 4000 euro/month while the Indian generic industry was able to produce an equivalent for 99 euro/month, making it accessible for patients in need. But Bayer started a court case to prevent this. Mr. Dekkers said: We did not develop a cancer medicine for Indians. We developed it for Western patients who can afford it'.

(Figure 1, Big Pharma Charges Unaffordable Prices for Medicines in India, infographic MSF)



The response of Manica Balasegaram of Médecins Sans Frontières (MSF's) Access to Medicines Campaign is that 'this statement sums up everything that is wrong with the multinational pharmaceutical industry today; drug companies, claiming to care about Global Health, do not act accordingly and are part of the problem instead of part of the solution'.¹ Instead, the pharmaceutical industry is profit-driven and very successful at that. The combined worth of the world's top five drug companies is twice the combined GDP of sub-Saharan Africa and according to IMS Health the global pharmaceutical industry is expected to rise to the worth of US\$1.1 trillion by 2014.

But from being widely admired for its integrity, noble ideals and altruism, the pharmaceutical industries reputation has sunk to being 'distrusted and devalued', with a 'broken image'.² According to a survey in 2012 in 56 countries the pharmaceutical industries reputation is at an all time low.³ The main reason people gave for their poor rating was the industries failure to help patients in low –and middle income countries to gain access to medicines– the general opinion held was that "profit comes before making people well".

Contrary to this survey, Hans Hogerzeil, former director of WHO's Essential Medicines and Pharmaceutical Policies department, stated in September last year that the pharmaceutical industry as a whole is making progress, and is becoming more organized in its approach to global access to medicines.⁴ This was based on the 2012 'Access to Medicine Index', in which the 20 largest pharmaceutical companies were assessed for their efforts in making drugs accessible to the world's poorest.

However Ellen 't Hoen, the world's foremost activist on the issue of global drug patents and human rights states that this progress has only been made due to 10 years of continued activism, with no or little impetus coming from the industry itself.⁵

Activism was kick-started and the term 'access to drugs' was coined in early 1998, when 41 drug companies sued South Africa, the country that had experienced an explosive spread of HIV/AIDS and until today has the highest number of cases worldwide. The legal fight was over a new law, under Nelson Mandela's regime, that would make low-cost copies of expensive Western anti-retroviral drugs available to patients. These drugs would prevent a certain death from AIDS, but were far too expensive for South African patients with a price tag of US\$10,000 to 15,000 per patient per year. The new law would radically change this situation and save millions of lives, but the opposition of Big Pharma was relentless. Only in April 2001, after a global outcry, the lawsuit was dropped. This was the start of the reversal of the HIV/AIDS epidemic in Africa - now, due to continued activism, antiretrovirals have become accessible for over five million people in the developing world.⁵

¹ Manica Balasegaram: Drugs for the poor, drugs for the rich—why the current research and development model doesn't deliver. Feb 13, 2014, British Medical Journal blog

² Devalued and Distrusted: Can the Pharmaceutical Industry Restore its Broken Image? John L. LaMattina, Feb 2013, ISBN: 978-1-118-48747-1

³ Corporate reputation of Pharma – the patient perspective. Feb 2014, Patient View Report.

⁴ Hans V Hogerzeil, Jayasree K Iyer, Lisanne Urlings, Tara Prasad and Sara Brewer. Is the pharmaceutical industry improving with regard to access to essential medicines? The Lancet Global Health 2, 3, 139-140 (March 2014)

⁵ E't Hoen, J Berger, A Calmy. Driving a decade of change: HIV/AIDS, patents and access to medicines for all. J Int AIDS Soc 14, 15, 2011

But today, history is repeating itself. The 17th of January this year, leaked documents revealed that Big Pharma had allocated 600,000 USD for a large-scale public relations campaign against South Africa's new plan to decrease drug prices in the country.⁶ The plan would modify the countries patent system in order to serve public health, and ensure that monopolies on drugs could no longer be extended by changing a formulation or combining two medicines into a single tablet, and then patenting this change. This practice of patent 'evergreening' is a long-known strategy of the industry in Europe and the US. It keeps drug prices artificially high as it postpones generic competition. The hidden agenda of Big Pharma was painfully exposed; they will go far to prevent South Africa from taking the lead once more. Africa is an emerging economy, with its rapidly growing cities offering a considerable future market for pricey drugs. Pharmaceutical spending in Africa may reach \$30 billion by 2016, from approximately \$18 billion at present. Big Pharma's strategy is based on keeping high prices firmly in place through holding on to intellectual property rights and patents in these emerging markets, to the disadvantage of the world's poor.

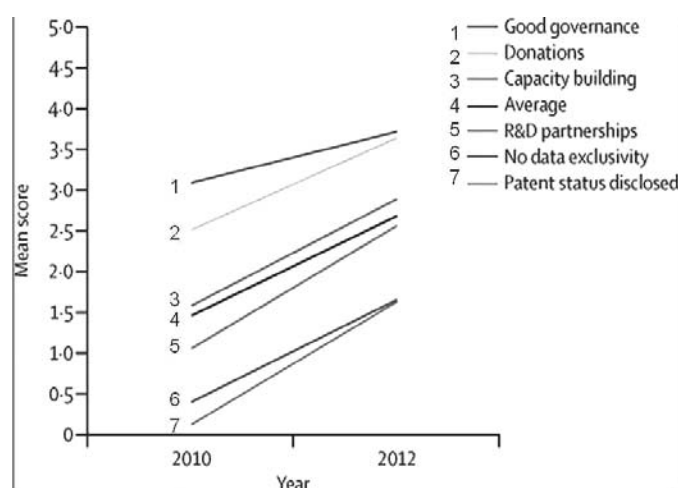
A similar legal fight on 'evergreening' took place half a year earlier in India. Novartis ('Caring and Curing') lost a six-year long battle after the Indian court ruled that small changes and improvements to a new cancer drug, called Glivec, were not enough reason to prolong its patent in India. This allowed Indian firms to immediately market cheap generic copies (Glivec costs over 2000 USD/month). In an interview before the ruling, Novartis threatened to stop supplying India with any new medicines if it did not get patent protection. "If the situation stays as it is now, all improvements on an original compound are not protectable and such drugs would probably not be rolled out in India", Paul Herrling, who headed the company's legal battle in India, told the Financial Times.⁷ "Why would we?"

Apart from the legal battles and the cajoling of governments of resource-poor countries, Big Pharma arguments that the exceedingly high prices of new drugs are justified because of their research and development (R&D) costs; lowering drug prices would endanger global medical innovation. Recently, a staggering price of 5 billion US\$ per drug was calculated based on quotes of drug companies.⁸ But there is a great lack of transparency in these quotes,

and they are often questioned, even by the industry itself; last year, GSK's Andrew Witty called a previously quoted \$1 billion figure "one of the great myths of the industry".⁹ MSF's Access to Medicines Campaign claims that globally, about half of R&D is not even financed by the industry, but subsidized by governments and philanthropic organizations.¹ The public-private partnership DNDi (Drugs for Neglected Diseases initiative) demonstrated that innovative drugs could be developed for 100-150 million US\$ – a fraction of the numbers used by the industry.¹⁰

In the 2012 Access to Medicine Index, the lowest scores were obtained for progress related to patents and data exclusivity.

(Figure 2, Changes in six core ATM indicators, 2010–12)⁴



Global access to drugs was most successfully increased by large scale drug donations. These have been the answer of Big Pharma to the world's heavy criticism. Drug donation

⁶ MSF urges South Africa to stand strong in defiance of aggressive pharma moves to delay change. Jan 20, 2014, MSF Access Campaign

⁷ Novartis warns India over drug patent. Andrew Jack and Amy Kazmin. Mar 31, 2013, Financial Times

⁸ The cost of creating a new drug now \$5 billion, pushing Big Pharma to change. Matthew Herper, Pharma and Health Care, www.forbes.com. Nov 8, 2013.

⁹ GlaxoSmithKline boss says new drugs can be cheaper. Ben Hirschler. Mar 14, 2013, www.reuters.com

¹⁰ Research & Development for Diseases of the Poor: A 10-Year Analysis of Impact of the DNDi Model. Press release DNDi, Dec 5, 2013. www.dndi.com

programs are tax deductible, don't have implications for drug pricing in general, and are now almost routinely undertaken as part of company strategy. Examples are "Merck's Gift," the program where billions of river blindness drugs were donated for Africa, Pfizer's donation of free or discounted fluconazole and other drugs for HIV in South Africa and GSK's commitment to donate albendazole tablets for the elimination of lymphatic filariasis worldwide. These initiatives have helped to create highly successful control programs, but laudable as they are, there are drawbacks - diseases for which the industry provides cures now dominate the public health agenda, whilst other, more difficult to tackle problems, such as diarrhea or maternal death during childbirth do not get the attention they deserve.

Apart from its Patents-Before-People policy, how are Big Pharma operating in poor countries?

Ben Goldacre is a British doctor and medical writer who published a best-seller in 2012 called 'Bad Pharma – how Drug Companies Mislead Doctors and Harm Patients' (the book was endorsed by the founder of the prestigious Cochrane Library in the UK).¹¹ In this book, Big Pharma's failings to protect public health benefits in the West are highlighted. He argues that aggressive marketing of superfluous or dangerous drugs, embezzlement of clinical data and lack of independent science and information are the rule instead of the exception, with regulations in Europe and the US being increasingly dominated and manipulated by the industry. The book gives examples where patient safety was knowingly compromised, and refers to the increasing number of clinical studies that are performed in developing countries to escape the strict regulations and high costs in the West. What would an in depth investigation reveal about the behavior of Big Pharma in developing countries, where regulations are not only much less strict, but in many cases not enforced? The thought is deeply unsettling.

In the last decade, popular fiction included some seething exposes on the greed and ruthlessness of Big Pharma in Africa, such as John Le Carre's book 'The Constant Gardener', made into a Hollywood movie in 2005. The author stated in the credits that "nobody in this story, and no outfit or corporation, thank God, is based upon an actual person or outfit in the real world, but I can tell you this, as my jour-

ney through the pharmaceutical jungle progressed, I came to realize that, by comparison with the reality, my story was as tame as a holiday postcard". The book was based on a real event that took place in Kano, Nigeria. During a severe meningitis epidemic and in a hospital overflowing with patients, Pfizer decided to test a new antibiotic, named Trovan. The drug was Pfizer's most promising at the time with projected annual sales of over a billion US\$ a year, but it was not yet approved in the USA. In animal tests it was shown that it might cause significant side effects in children such as joint disease, bone deformation and liver damage. Yet, the trial in Nigeria tested the drug in children with Pfizer cutting serious ethical corners; most parents of the children who were enrolled could not speak or read English, and did not understand that the proposed treatment was experimental and that a safe, approved treatment was offered in the same hospital for free. After two weeks the trial was finished and the Pfizer team left Kano, to never return for follow-up evaluations. Of 200 children, 11 died and others became paralyzed, deaf or blind (Pfizer later reached a settlement of 75 million US\$ with the Nigerian authorities). Pfizer filed for US FDA approval for Trovan's use in children based on the Kano trial, but failed to obtain it. However, the drug was approved for adults and entered the US and European markets in 1998 where it immediately became a top-selling drug. But in 1999, less than a year later, it became apparent that the drug caused serious liver damage in adult patients. Trovan was withdrawn from the European market and is only allowed for a small group of selected patients in hospitals and nursing homes in the USA.

A chilling book written by the famous Swedish detective writer Henning Mankell, named 'Kennedy's Brain', described the activities of a multinational pharmaceutical company in an unacknowledged clinic, set in a remote corner of Mozambique. In this clinic, HIV drugs were tested on infected victims without their consent, and healthy Africans were unwittingly infected with HIV and held in captivity so that the new drugs could also be tested on those who were recently infected. The writer, who now lives in Mozambique and works with charities that help people living with HIV, stated in his book that he could not write

¹¹ Bad Pharma – how Drug Companies Mislead Doctors and Harm Patients. Ben Goldacre, Sept 2012, ISBN: 978-0-00-735074-2

non-fiction about what he knew of the situation in Africa because few would take him seriously.

We may never know the truth of what actually happened in these and other remote settings. Surely the question what harm Pharma's corporate greed can do in an environment where there is an absence of regulations is a very poignant one. For one, the active marketing of drugs in developing countries that have been disapproved for use in the West has been well documented.¹²

Big Pharma's aggressive marketing practices themselves are a subject of much debate and public outrage.¹¹ A recent statement by GSK ('Do More, Feel Better, Live Longer'), introducing a new sales scheme for pharmaceuticals, said the following:

'Our new (compensation) programme will have no individual sales targets. Instead, GSK's sales professionals who work directly with prescribing healthcare professionals will be evaluated and rewarded for their technical knowledge, the quality of the service they deliver to support improved patient care and the overall performance of GSK's business'. The programme bases compensation for sales professionals who work directly with prescribing healthcare professionals on a blend of qualitative measures and the overall performance of their business, rather than the number of prescriptions generated'.¹³

This directly reflects current practice: as in any other industry, sale targets are paramount. This statement of GSK was published soon after it received a record 3 billion US\$ fine for marketing drugs beyond their authorized uses. Fines of this magnitude for off-label promotion are common among Big Pharma: Pfizer ('Working for a Healthier World') was fined US\$ 2.3 billion in 2010, and Abbott ('A Promise for Life') US\$ 1.5 billion in 2012. In 2013 Chinese authorities announced that in the last 5 years, the bribes and sexual favors that GSK had provided to managers, doctors, hospitals and others who prescribed GSK drugs amounted to nearly 0,5 billion US\$.

Probably one of the direst consequences of an entirely market-driven drug industry is the lack of investment into drugs for diseases that predominantly affect poor people in poor countries and for which there is little or no market

potential. There is no financial incentive to invest in R&D for these so-called neglected diseases, for which in many cases no safe and effective drugs exist. According to the World Health Organization (WHO), Sub-Saharan Africa has 11% of the world's population, yet it accounts for 24% of the global disease burden. A study in 1999 demonstrated that of 1,393 new medicines launched globally between 1975 and 1999, only 13 (1%) were for tropical infectious diseases. But as 10 of these 13 drugs were developed for veterinary or military purposes, only three that were the result of genuine efforts to create drugs for these neglected diseases.¹⁴ There is little indication that the situation is improving; just 4% of new drugs and vaccines approved between 2000 and 2011 were for neglected tropical diseases.¹⁵ Some recent progress has been made, such as the r 'London Declaration on Neglected Tropical Diseases', a large scale coordinated initiative by government, industry and other stakeholders, launched in January 2012. It aims to eradicate 10 neglected diseases by 2020 and provide 785 US\$ to support R&D. This initiative was officially endorsed by the 13 leading pharmaceutical companies; however, one of these, AstraZeneca ('Life Inspiring Idea's), recently announced it was pulling out of all early stage R&D for malaria, tuberculosis and neglected tropical diseases. The company stated it will only invest in drugs for cancer, diabetes, and high blood pressure; the chronic diseases of the affluent.¹

A voluntary fund, to which pharmaceutical corporations would contribute an agreed percentage of their profits for R&D for neglected diseases, has been proposed as a potential solution to this problem. But as yet, attempts at developing codes of conduct that rely on voluntarism have

¹² See, for example: Dipryone, a drug no one needs, BukoPharma <http://www.en.bukopharma.de/uploads/file/Archiv/Dipryone-ADrugNo-oneNeeds.pdf>

¹³ GSK announces changes to its global sales and marketing practices to further ensure patient interests come first. Press release GSK, Dec 17, 2013. www.gsk.com

¹⁴ Fatal Imbalance. The Crisis in Research and Development for Drugs for Neglected Diseases. DNDi. http://www.dndi.org/images/stories/press_kit/rnd/pdfs/fatal_imbalance_2001.pdf

¹⁵ B Pedrique, N Strub-Wourgaft, C Some. The drug and vaccine landscape for neglected diseases (2000-11): a systematic assessment, *Lancet* 1, 6, 2013

not been successful in ensuring accountability. The term 'corporate social responsibility' (CSR) became popular in the 1960s, and is now routine in business strategy, but it is commonly acknowledged that it is failing to deliver for both companies and society. A recent report by Mc Kinsey outlined that 'traditional CSR' relies on three tools: a full-time CSR team in the head office, some high-profile (but relatively cheap) initiatives, and a glossy annual review of progress; and that companies often see CSR as an exercise in protecting their reputation and get away with irresponsible behavior.¹⁶ CSR is not by any stretch adequate to ensure global access to drugs. As in all other industries, Pharma's corporate strategy does not include a human rights agenda. Even the idea that businesses have obligations regarding human rights is relatively new and controversial. Although corporate accountability standards, such as the UN Human Rights Norms for Business, have been endorsed by many stakeholders, they are not likely to become legally enforceable.

Recent studies have given insight in the underlying mechanism of corporate greed and the unprecedented levels of economic inequality of these times. The US Berkeley scientist Paul Piff demonstrated via multiple experiments that increased wealth and status in society lead to increased self-focus and, in turn, decreased compassion, altruism, and ethical behavior.¹⁷ The experiments showed, for example, that those who drive expensive cars are far more inclined to break the law and even that people considering themselves rich will take twice as much candy from a jar that was specifically identified as being reserved for children than the less well-off. The more wealthy one is, the more inclined to bribe, promote unethical behavior, steal and lie; the more severe inequality becomes, the more entitled the privileged will feel and the less likely to share resources. These experiments however also showed how small psychological interventions can fully restore empathy and egalitarian behavior. A direct confrontation with the needs of others, for example via a short video on child poverty, will generate compassionate behavior in equal measure in the rich and the poor. Indeed, as the world becomes more transparent through internet, twitter and whistleblowers, and global awareness of inequity and the suffering it causes is increasing, its effect becomes apparent in society. Initiatives where the extremely wealthy dedicate a large part of their resources to charity are be-

coming more and more common. The Bill and Melinda Gates Foundation and the Giving Pledge, in which more than 100 of America's wealthiest pledged half of their fortune to combat inequity, are examples of the very privileged acting on the impulse of compassion. Why are big corporations, and specifically Big Pharma, lagging behind? Is the simple answer that its decision-makers are emotionally disconnected from the reality on the ground that their company strategies create?

BOX

WHO, 10 June 2013: "I am deeply concerned by two recent trends. The first relates to trade agreements. Governments introducing measures to protect the health of their citizens are being taken to court, and challenged in litigation. This is dangerous. The second is efforts by industry to shape the public health policies and strategies that affect their products. When industry is involved in policy-making, rest assured that the most effective control measures will be downplayed or left out entirely. This, too, is well documented, and dangerous."

Dr Margaret Chan
Director-General of the World Health Organization
Opening address at the 8th Global Conference on Health Promotion
Helsinki, Finland

¹⁶ Beyond corporate social responsibility: Integrated external engagement. John Browne and Robin Nuttall. March 2013. www.mckinsey.com

¹⁷ See for all publications of Dr Piff: paulpiff.wix.com/paulpiff and for a summary of his work: http://www.ted.com/talks/paul_piff_does_money_make_you_mean

BOX

Big Pharma slogans

Merck. Where patients come first.
Pfizer. Working for a healthier world.
Sanofi-Aventis. Because health matters.
GlaxoSmithKline. Do more, feel better, live longer.
Bayer. Science for a better life.
Novartis. Caring and Curing.
Astra Zeneca. Life Inspiring Idea's.

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